Clinical Approach dignosis of CKD Patient

By

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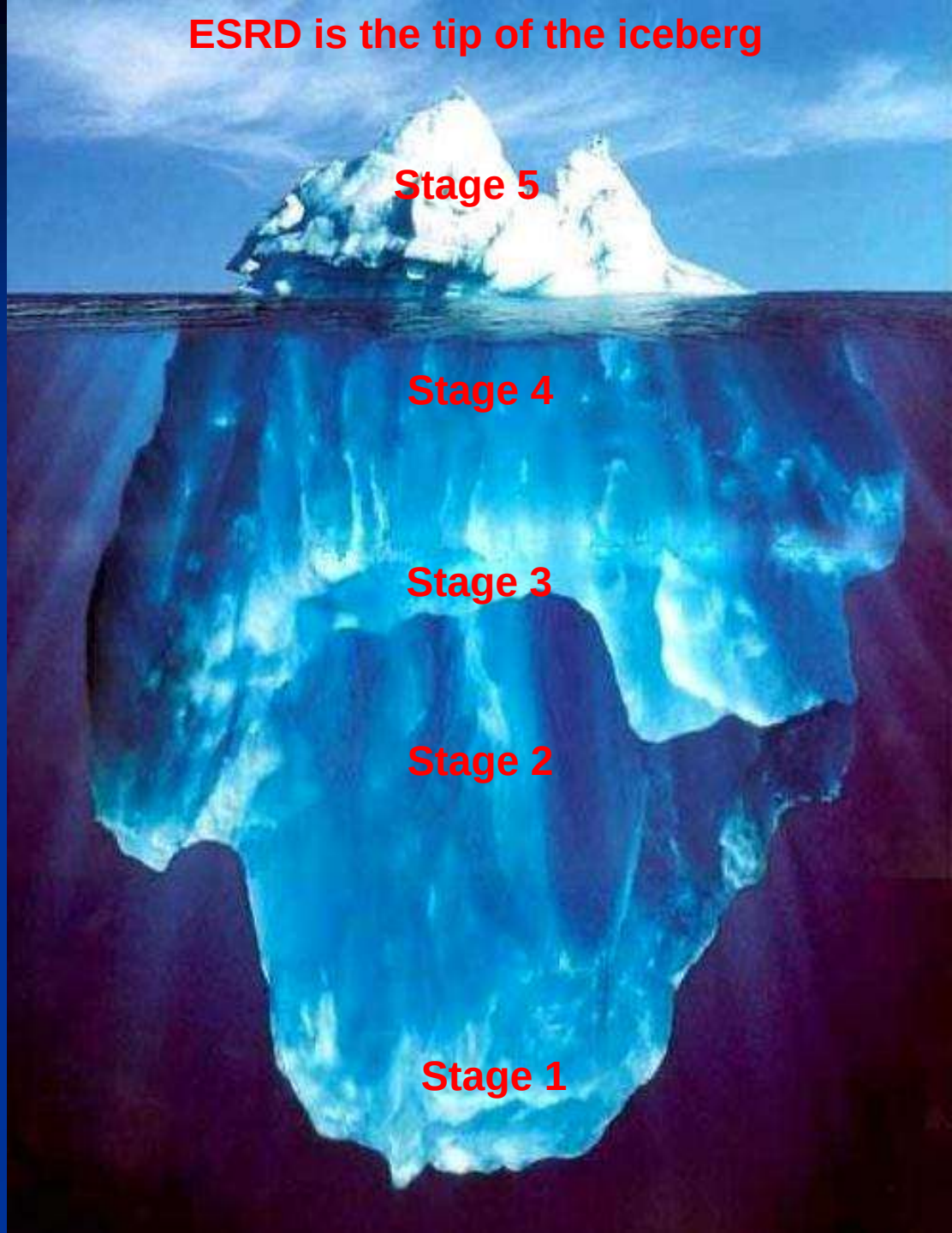
End-stage renal disease (ESRD) is a major health problem associated with considerable increase in morbidity and mortality and with decreased in quality of life



Definition and stages of CKD

Early Detection and diagnosis of CKD Patients

STAGES OF CHRONIC KIDNEY DISEASE (CKD)

Stage	Description	GFR (ml/min/1.73 m^2)
1	Kidney damage with normal of ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60-89
3	Moderate ↓ GFR	30-59
4	Severe ↓ GFR	15-29
5	Kidney Failure	< 15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR < 60 ml/min/1.73 m^2 for ≥ 3 months.

Kidney damage is defined as pathological abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

Definition

The National Kidney Foundation (NKF) defines chronic kidney disease as kidney damage or a GFR of < 60 mL /min/1.73 m2 body surface area) for ≥ 3months.

This GFR corresponds with a serum creatinine concentration higher than 1.5 mg per dL in men and higher than 1.3 mg per dL in women.

Risk factors for CKD

1) Susceptibility factors; old age, family history of CKD, low birth wt(renal mass), racial, low economic status).

2) Initiation factors; DM, HTN, autoimmune dis., infections, UTI, stones, obstruction, drugs.

3) Progression factors; Proteinuria,HTN, hyperglycemia, hyperlipidemia, obesity, highprotein diet, smoking, anemia, metabolic acidosis, phosphate retention, type of the underlying dis.

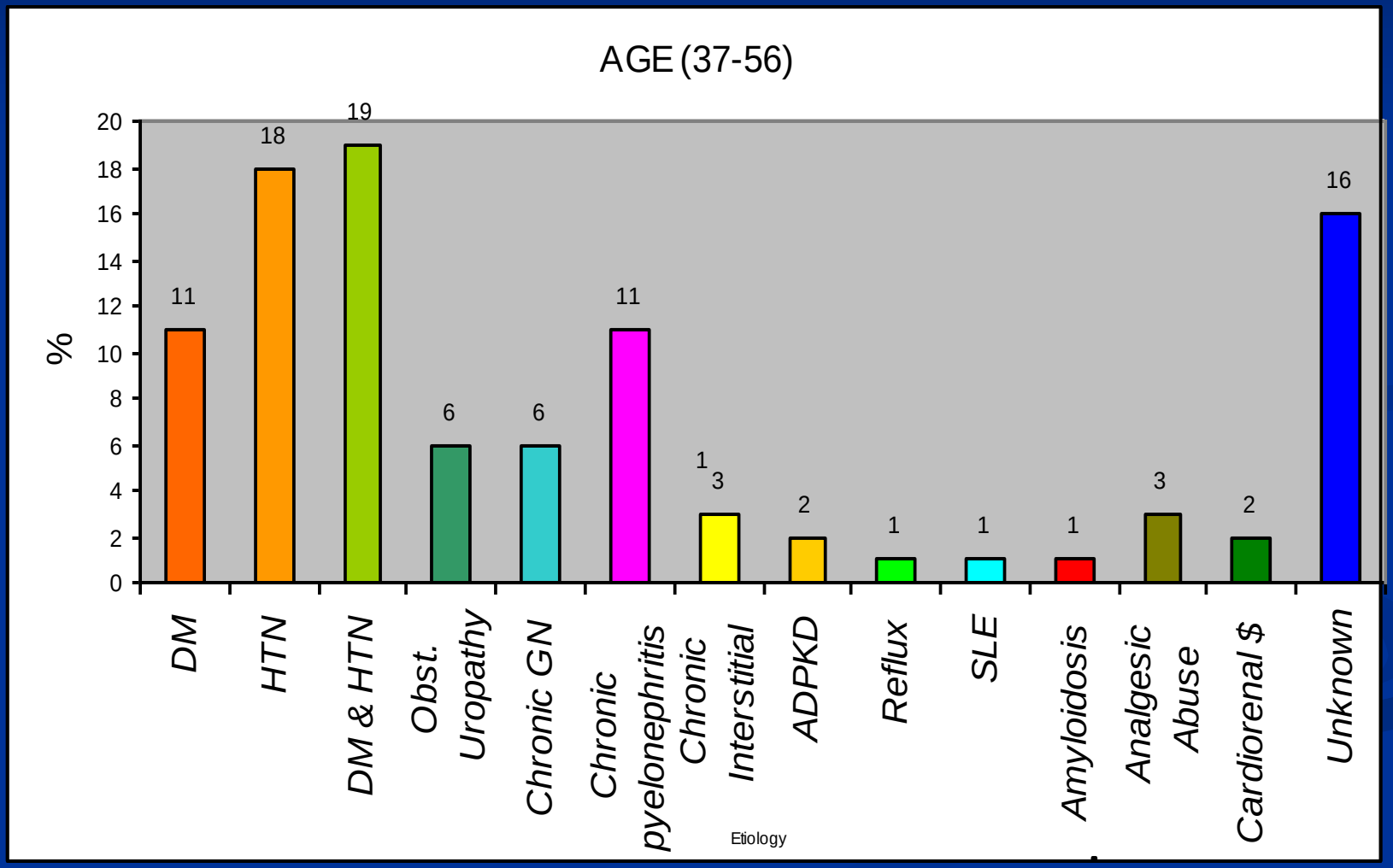
e.g. lower rate of progression in Tubulo interstial diseases.

4) End stage factors (pt mortality & morbidities); late referral, adequacy of dialysis, temporal vascular access, nutritional status, s. alb., anemia, CVD).

Patients at risk for developing CKD

* Hypertension
* Cardiovascular disease
* Diabetes mellitus
* Age above 60 years
* Family history of kidney disease
* Recurrent urinary tract infections
* Exposure to certain drugs e.g.NSAIDs, antibiotics and contrast agents or chemicals.

- Diabetes and hypertension together followed by hypertension alone are the most common causes of CKD at the age of 37-56 years.



Pathogenesis of CKD progression

1) Type & activity of the initial disease ; faster progression with HTN, DM, GN, ADPKD than T.I diseases.

2) secondary factors ;

*** Angiotensine II, Aldosterone & Intraglomerular Hypertrophy**

*** Proteinuria**

*** Higher blood pressure**

*** Hyperlipidemia & Lower serum HDL cholesterol**

*** Hyperglycemia.**

*** Smoking, high protein, high salt diet, obesity.**

*** Iron toxicity**

*** Phosphate retention & Hyperuricemia**

*** Metabolic acidosis**

*** Anemia**

*** Corticosteroids**

*** Black race, male gender, Genetic factors.**

Screening and early detection of chronic kidney disease

The National Kidney Foundation criteria for diagnosis of CKD are :

1) **Kidney damage** for greater than or equal to 3 months, as defined by structural or functional abnormalities of the kidney , with or without decreased glomerular filtration rate , manifest by either :
a. Pathological abnormalities or
b. Markers of kidney damage , including abnormalities in the composition of the blood or urine , or abnormalities in imaging tests
2) **Glomerular filtration rate** less than 60ml/min/1.73 m2 for greater than or equal to 3 months , with or without kidney damage.

Kidney damage

Chronic kidney disease is diagnosed by markers of damage as:

1) Proteinuria; defined by the presence of urinary albumin > 300 mg per 24 hours or in a ratio of more than 200 mg of proteins to 1 g of creatinine (0.2).

2) Urine sediments (tubular casts, cells).

3) Blood or urine chemistry due to altered tubular functions e.g. RTA.

4) Imaging; hydronephrosis, asymmetry, small, PCKD.

EVALUATION OF PROTEINURIA

Proteinuria is the second most important parameter in the clinical evaluation of kidney function. There are several reasons for this.

1) For many patients with early kidney disease, the GFR may be normal and there is
no upward increase in serum creatinine.

2) Proteinuria is the single most important risk factor for future loss of kidney function.

3) Among patients with CKD , proteinuria is an important and independent risk factor for cardiovascular disease and mortality. This may be because leakage of protein into the urine reflects generalized endothelial damage and capillary injury.

Proteinuria

Determination of albumin in a spot urine sample is sufficient for the detection of proteinuria in most patients.

It should be borne in mind that the urine dipstick is specific for albumin and does not detect paraproteinuria.

In the case of a positive dipstick analysis, the total protein to creatinine (P/C) ratio in a spot urine sample should be measured.

* urine dipstick analysis
It should be performed using an untimed spot urine sample to screen presence of protein, red blood cells (RBC) and white blood cells (WBC).

RBC/WBC dipstick

Abnormalities other than proteinuria can be present in CKD prior to a noticeable reduction in the glomerular filtration rate (GFR).

If positive for WBC or RBC, a microscopic analysis of urinary sediment should be performed on an untimed urine sample.

SPOT URINE SAMPLES VERSUS 24-HOUR URINE COLLECTIONS TO QUANTIFY PROTEINURIA

The methods most familiar to clinicians for proteinuria assessment are dipstick urinalysis and 24-hour urine collection. The former, however, only provides relatively crude quantification of the concentration of protein and thus is affected by urinary dilution. The latter is susceptible to the same overcollection and undercollection errors that plauge 24-hour urine quantification of creatinine clearance

* This was demonstrated by Rodby et al. in the US multicentre study on the usefulness of a random urine specimen P/C ratio in predicting urine protein excretion (24 UP) in patients with diabetic nephropathy treated with angiotensin-converting enzyme (ACE) inhibitors.
* When the P/C ratio (g/g) was 1, the interval of the ‘mean±1 SD’ of proteinuria ranged from 0.7 to 1.8 g/24 h.
when the P/C ratio was 6, the interval ranged from 3.4 to 9 g/24 h, and when the ratio was 9, that interval ranged from 4.8 to 13.0 g/24h.
* Thus, standard deviations associated with predictions when measured by a P/C ratio were large, especially at the higher 24 UP values.
* Therefore, in monitoring patients with CKD, a P/C ratio in urine samples regularly should be combined with timed urine collections.

1st Work up of proteinuria

- Urinalysis
- Urine sample
- Urine protein by dipsticks

Glucose.
Urobilinogen.
Bilirubin.
Ketones.
Specific gravity.
pH.
Nitrite.
Leukocyte esterase.
blood
Protein.

False +ve

High urine PH>8
with gross hematuria.
in the presence of penicillin, sulfonamides or tolbutamide.
with pus, semen or vaginal secretions.

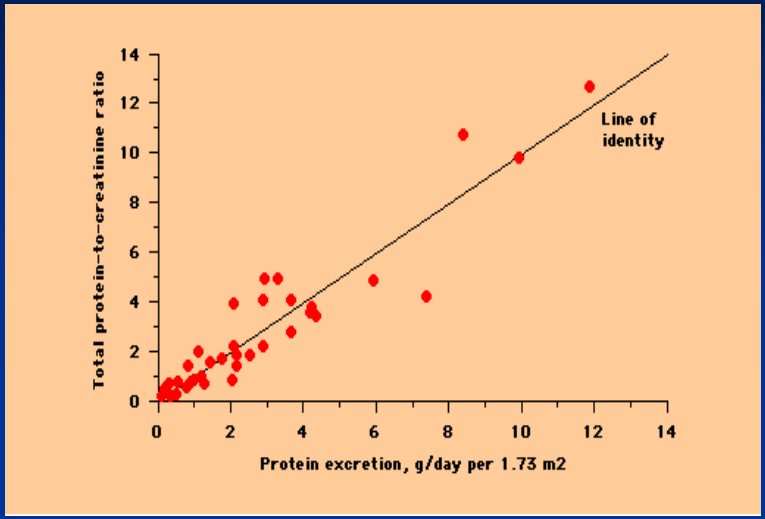
False –ve

Small amount of albumin: microalbuminuria
Large amount of non albumin protein

This method preferentially detects albumin and is less sensitive to globulins or parts of globulins or (heavy or light chains or Bence Jones proteins).

Laffeyette et al., 1996

Quantitative test



Protein creatinine Vs Albumin creatinine

Equivalent to 24h urinary protein	Equivalent to 24h urinary albumin.
Normally <150 mg/gm, Or 0.15 mg/mg.	Normally <30mg/gm
>0.2 mg/mg considered proteinuria	Microalbuminuria: 30-299 (false –ve test)
	Macroalbuminuria:≥300

Unites is important, if creatinine mmol x 0.088

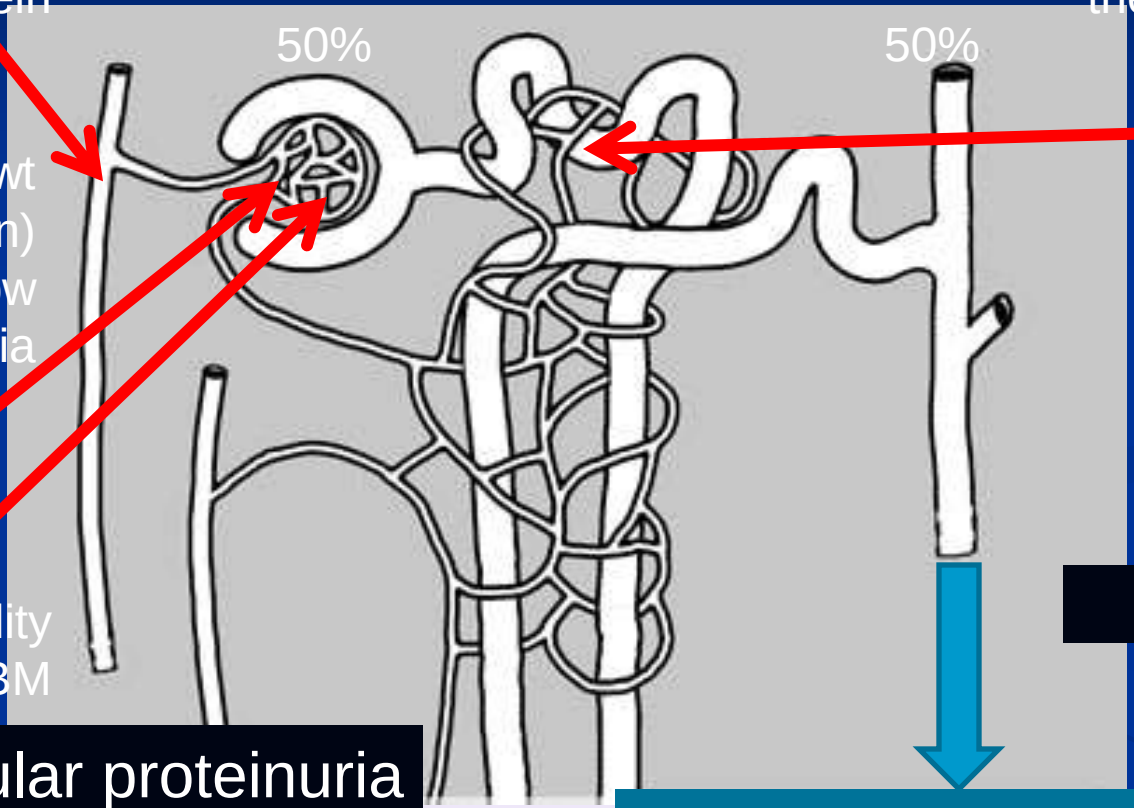
Protein excretion rate

Plasma protein

(if low mol wt protein) Overflow proteinuria

GFR

Permeability GBM



the proximal tubule

The ability of the proximal tubule to excrete , metabolize and reabsorb any filtered proteins

Tubular proteinuria

Glomerular proteinuria

The permeability of the glomerular basement membrane
Primary or secondary glomerulopathy

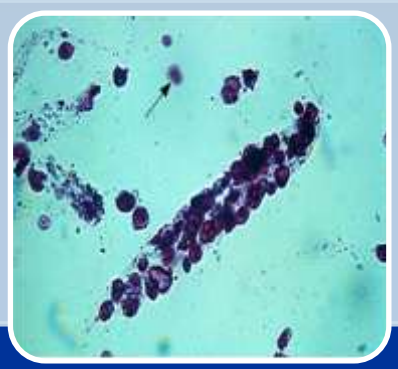
N urinary protein < 0.15 g per day (15% albumin)
N urinary albumin <30mg/gm creatinine
>0.2 gm proteinuria

Cause of Proteinuria (bland urinary sediment)Related to Quantity

Daily protein excretion	cause
0.15 to 2.0 g	Mild glomerulopathies Orthostatic proteinuria (0.15-<2gm) Tubular proteinuria Overflow proteinuria
2.0 to 4.0 g	Usually glomerular
>4.0 g	Always glomerular

Adapted with permission from McConnell KR, Bia MJ. Evaluation of proteinuria: an approach for the internist. Resident Staff Phys 1994;40:41-8.

DD of urinary cast

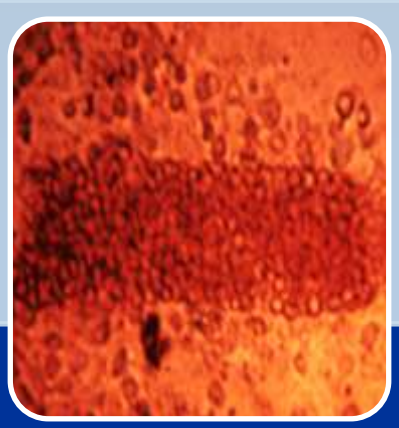


Epithelial cells casts

Acute tubular necrosis,

Pyelonephritis.

Nephrotic syndrome.



Red cell casts

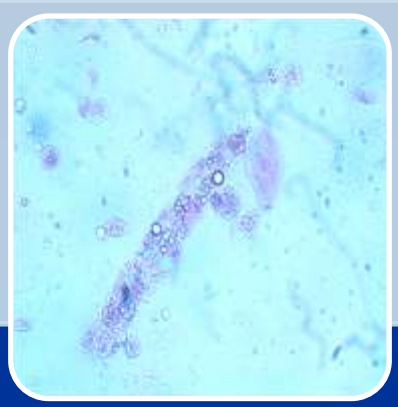
glomerulonephritis or vasculitis

White cell casts +

pyuria

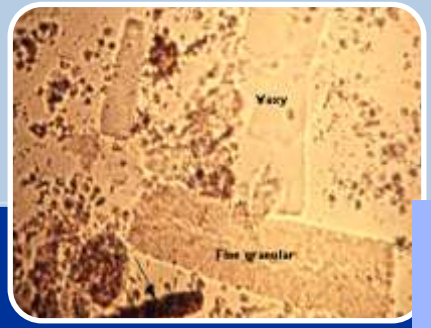
tubulointerstitial disease

acute pyelonephritis.

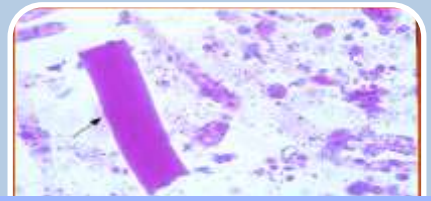


Fatty cast

proteinuria

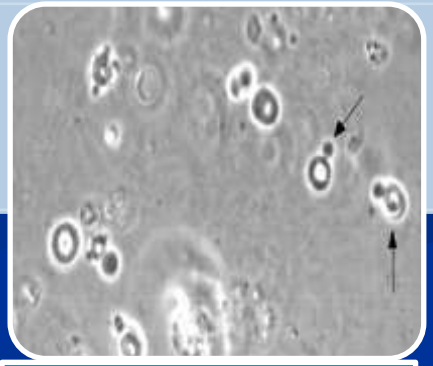


Granular cast



Advanced renal failure

Waxy cast



Dysmorphic RBCs

Imaging studies are recommended in patients who are at risk for chronic kidney disease because of

* Complicated urinary tract infections.
* Urinary tract stones or obstruction and vesicoureteral reflux.
* Family history of polycystic kidney disease.

Ultrasonography is particularly useful for detecting several of these conditions, and it does not involve exposure to radiation or contrast media.

IMAGING STUDIES

Renal ultrasound

Is particularly helpful for diagnosis some cases of CKD [ie , polycystic kidney disease (PKD), obstructive uropathy] and for distinguishing acute from chronic kidney disease. The presence of symmetrically small (<8.5 cm) Kidneys supports the diagnosis of CKD ,whereas the occurrence of normal-sized kidneys favors an acute rather than a chronic process. There are exceptions, however, as some causes of CKD are associated with normal-sized or even enlarged kidneys, including diabetes , PKD , and amyloidosis. Other imaging studies may help determine the cause of CKD.

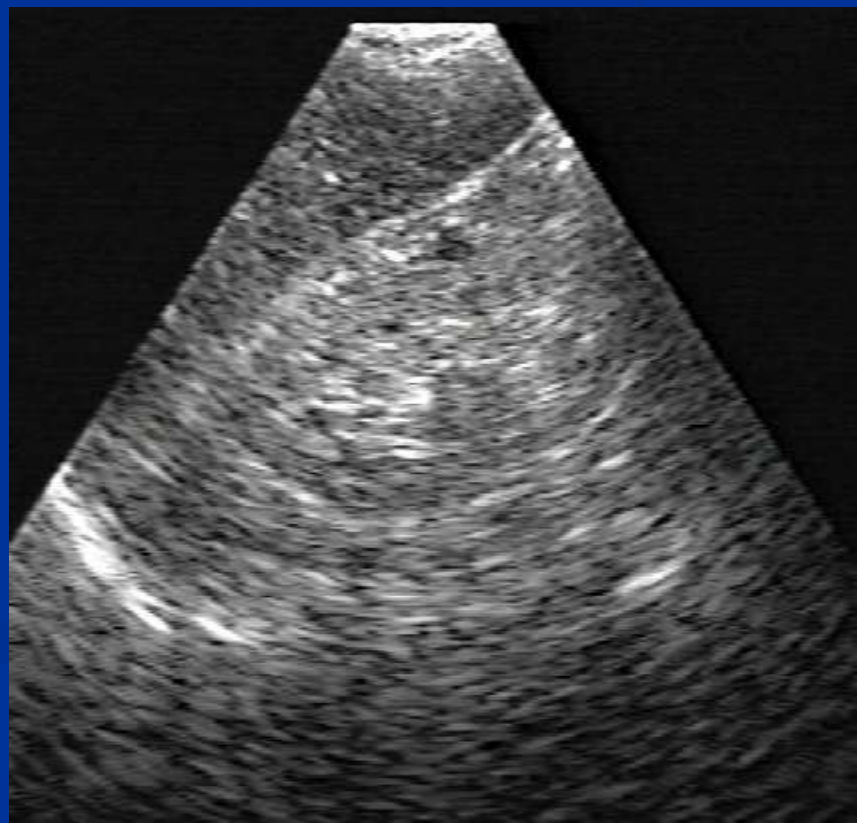
Duplex Doppler ultrasound of the renal arteries, Renal scintigraphy, and magnetic resonance angiogrphy are useful in patients in whom renovascular ischemic disease is suspected.

Voiding cystourethrography is helpful to rule out reflux nephropathy.

Computed tomography allows for assessment of kidney stone activity and for evidence of papillary necrosis.

Normal Kidney

ESRD Kidney



GFR

GFR (Creatinine Clearance)

- GFR = [UCr x V]/SCr.
- 24h urine collection.
- Increased tubular secretion of creatinine (CKD)……Over estimation of GFR.

Formulae for estimating GFR

Cockcroft-Gault Formula

Male

$$C_{cr} = \frac{(140 - \text{age}) \times \text{weight}}{72 \times P_{cr}(\text{mg/dl})} \quad \text{or} \quad C_{cr} = \frac{(140 - \text{age}) \times \text{weight}}{0.814 \times P_{cr}(\mu\text{mol/l})}$$

Female

$$C_{cr} = \frac{(140 - \text{age}) \times \text{weight} \times 0.85}{72 \times P_{cr}(\text{mg/dl})} \quad \text{or} \quad C_{cr} = \frac{(140 - \text{age}) \times \text{weight} \times 0.85}{0.814 \times P_{cr}(\mu\text{mol/l})}$$

MDRD Study Equation (Four-Variable Equation)

$$\text{GFR (ml/min/1.73 m}^2) = 186 \times P_{cr}(\text{mg/dl})^{-1.154} \times \text{Age}^{-0.203} \times 0.742 \text{ (if female)} \times 1.210 \text{ (if black)}$$

or

$$\text{GFR (ml/min/1.73 m}^2) = 186 \times \left[\frac{P_{cr}(\mu\text{mol/l})}{88.4}\right]^{-1.154} \times \text{Age}^{-0.203} \times 0.742 \text{ (if female)} \times 1.210 \text{ (if black)}$$

MDRD Study Equation with Standardized Serum Creatinine (Four-Variable Equation)

$$\text{GFR (ml/min/1.73 m}^2) = 175 \times \text{Standardized } P_{cr}(\text{mg/dl})^{-1.154} \times \text{Age}^{-0.203} \times 0.742 \text{ (if female)} \times 1.210 \text{ (if black)}$$

or

$$\text{GFR (ml/min/1.73 m}^2) = 179 \times \left[\frac{\text{Standardized } P_{cr}(\mu\text{mol/l})}{88.4}\right]^{-1.154} \times \text{Age}^{-0.203} \times 0.742 \text{ (if female)} \times 1.210 \text{ (if black)}$$

Recognizing Renal Failure

*GFR is the standard indicator of renal function.
Normal values for GFR are 130±15 mL/minute in males and 120±15 mL/minute in females.
*GFR declines with age at a rate of about 10 mL/minute for each decade beyond 40 years,
*expected values (in mL/minute) are
100 for those in their 40s,
90 for those in their 50,
80 for those in their 60s,
70 for those in their 70s

GLOMERULAR FILTRATION RATE:

*The most important parameter in the clinical evaluation of kidney function is the glomerular filtration rate (GFR) , which is generally accepted as the best overall index of kidney function.

*A chronically low GFR by itself (less than 60 ml/min/1.73 m) is sufficient to make the diagnosis of CKD , regardless of the presence or absence of other markers of kidney damage.

*Measured GFR is the sum of all the single nephron glomerular
filtration rates in both kidneys.

*GFR remains the cornerstone of the clinical evaluation of kidney function .

WHY NOT USE SERUM CREATININE ALONE TO EVALUATE KIDNEY FUNCTION ?

CREATININE

1) Molecular weight 113 Daltons
2) Endogenously produced by muscle and excreted by the kidney . Therefore, reduction in GFR leads to an increase in SCR
3) Serum creatinine is easy and cheap to measure and no urine collection is needed.

One known problem is that renal creatinine clearance is not the same as GFR because creatinine is not an ideal filtration marker . It is not only filtered in the glomeruli but also actively secreted by renal tubules . Therefore, creatinine clearance tends to overestimate GFR .

More importantly , serum creatinine often does not reflect underlying GFR because SCr is a function not only of creatinine clearance (which reflects kidney function) but also creatinine production (which largely reflects muscle mass).

Therefore, the same SCr can represent very different underlying glomerular filtration rates in individuals because of muscle mass differences.

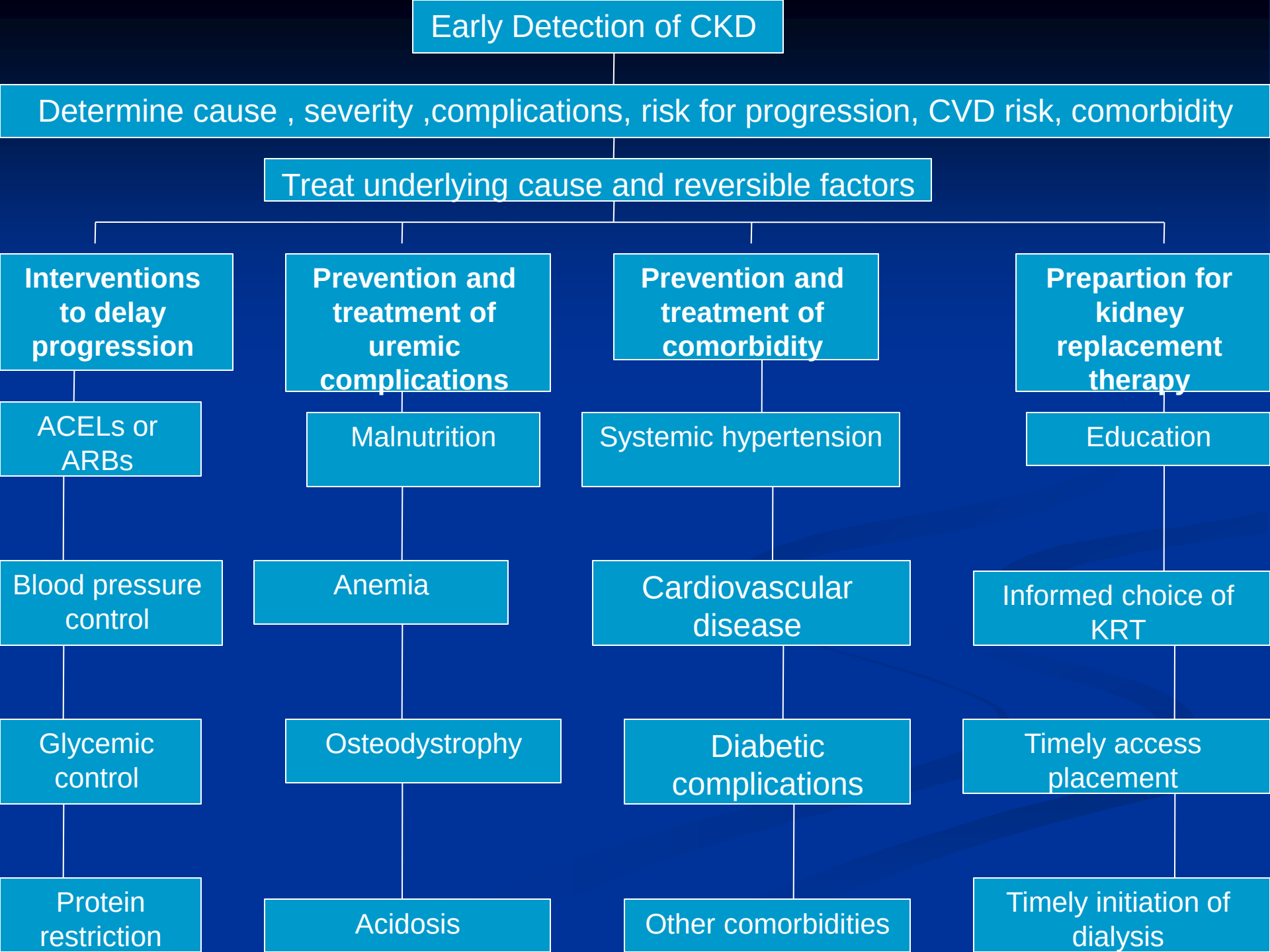
Clinical diagnosis

System	Clinical Manifestations
Skin	Paleness and hyperpigmentation Echymosis and hematomas Pruritus Skin neccrosis (calciphylaxis) Bullous lesions
Cardiovascular	Volume overload and systemic hypertension Accelerated atherosclerosis and ischemic heart disease Left ventricular hypertrophy Heart failure Rhythm disturbances Uremic pericarditis
Neurologic	Cerebrovascular accidents Encephalopathy Seizures Peripheral and autonomic neuropathy
Gastrointestinal	Anorexia Nausea and vomiting Malnutrition Uremic fetor Inflammatory and ulcerative lesions Gastrointestinal bleeding

System	Clinical Manifestations
Hematologic	Anemia Leukocyte and immune system dysfunction(tendency to infections) Platelet dysfunction(bleeding diathesis)
Bone	Renal osteodystrophy Growth retardation in children Muscle weakness Amyloid arthropathy secondry to β2-microglobulin deposition
Endocrine	Sexual dysfunction Infertility in women Glucose intolerance due to insulin resistance Hyperlipidemia
Laboratory	Hyponatremia (if excessive water intake) Hyperkalemia Hyperphosphatemia Hypocalcemia Hypermagnesemia Hyperuricemia Metabolic acidosis

Management of CKD

1)Early recognition of renal failure;
2)Detection and correction of reversible causes of renal failure
3)Institution of interventions to delay progression of renal failure;
4)Monitoring the progression of renal failure
5)Avoidance of additional renal injury;
6)Treatment of complications
7)Planning for renal replacement therapy


Early Detection of CKD
Determine cause , severity ,complications, risk for progression, CVD risk, comorbidity
Treat underlying cause and reversible factors
Interventions to delay progression
Prevention and treatment of uremic complications
Prevention and treatment of comorbidity
Prepartion for kidney replacement therapy
ACELs or ARBs
Malnutrition
Systemic hypertension
Education
Blood pressure control
Anemia
Cardiovascular disease
Informed choice of KRT
Glycemic control
Osteodystrophy
Diabetic complications
Timely access placement
Protein restriction
Acidosis
Other comorbidities
Timely initiation of dialysis


Thank You